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| 09/211,297 | 12/14/1998 | WILLIAM J. BOYLE | A-451M | 7253 |

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| EXAMINER | |
|---|---|
| SZPERKA, MICHAEL EDWARD | |
| **ART UNIT** | **PAPER NUMBER** |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/211,297 | BOYLE, WILLIAM J. | |
| | Examiner | Art Unit | |
| | Michael Szperka | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *93-103* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *93-103* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/14/08, 10/14/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. Applicant's response received October 14, 2008 is acknowledged.

Claims 1-92 have been canceled.

Claims 93-103 have been added.

Claims 93-103 are under examination in the instant office action.

2. The declaration of John K. Sullivan submitted under 37 CFR 1.132 is acknowledged and will be discussed with the rejections of record.

### *Information Disclosure Statement*

3. The IDS forms received October 14, 2008 are acknowledged and have been considered.

### *Claim Rejections - 35 USC § 102/103*

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The rejection of claims 82-92 under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Gorman et al. (US Patent No. 6,242,586, of record as reference B on form 892 dated March 27, 2003, see entire document) has been rendered moot by applicant's cancellation of said claims as part of the response received October 14, 2008.

The prior grounds of rejection have not been applied to the newly presented claims because applicant has supplied evidence in the response received October 14, 2008, including the declaration by John K. Sullivan, that not all antibodies which bind 499E9/OPGbp/OPGL/RANKL and inhibit its interaction with OPG/RANK bind to 499E9/OPGbp/OPGL/RANKL at either the BB' or the EF loop. Specifically, antibodies have been generated that block activity but do not bind to either BB' or EF (see also Example 10 of 09/791,153). Further, since the prior art did not recognize that said loops were important for ligand-receptor interactions, a person of ordinary skill in the art would not have been motivated to make antibodies that bound said loops on 499E9/OPGbp/OPGL/RANKL.

7. The rejection of claims 82-92 under 35 U.S.C. 103(a) as being unpatentable over Anderson (US patent 6,740,522, of record as reference A10 on the 5/14/07 IDS) in view of WO 93/12227 (of record as reference BC on the 3/25/99 IDS) has been rendered moot by applicant's cancellation of said claims as part of the response received October 14, 2008.

The prior grounds of rejection have not been applied to the newly presented claims because applicant has supplied evidence in the response received October 14, 2008, including the declaration by John K. Sullivan, that not all antibodies which bind 499E9/OPGbp/OPGL/RANKL and inhibit its interaction with OPG/RANK bind to 499E9/OPGbp/OPGL/RANKL at either the BB' or the EF loop. Specifically, antibodies have been generated that block activity but do not bind to either BB' or EF (see also Example 10 of 09/791,153). Further, since the prior art did not recognize that said loops were important for ligand-receptor interactions, a person of ordinary skill in the art would

not have been motivated to make antibodies that bound said loops on 499E9/OPGbp/OPGL/RANKL.

***Double Patenting***

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Applicant has cancelled all previously pending claims via the amendment filed October 14, 2008. However, the previously identified issues remain and thus rejections of the newly presented claims on the same grounds identified in prior office actions have been set forth below.

10. Claims 93-103 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of US Patent 7,364,736. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of issued patent anticipate the instant invention. Specifically, the issued claims are drawn to a specific antibody species recited by SEQ ID number whereas the instant claims are drawn to a broad genus of antibodies which comprise the same functional properties as the antibodies of the issued claims.

11. Claims 93-103 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-20, 22, 23, 25,

27, 29, 31-34, 36-38, 40, 42-50, 52, 59, 60, 62, 64-67, and 76-87 of copending Application No. 10/408,901. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of copending application 10/408,901 anticipate the genus of antibodies claimed in the instant invention because the copending claims recite antibodies of a specified heavy and light chain sequence. Note that these antibodies are claimed as being fully human (see particularly claims 49, 59, 60, 62, 64-67, and 76-87). Note also that the specification of the copending application discloses on page 70 that the antibodies of the copending application bind human OPGbp.

This is a provisional obviousness-type double patenting rejection.

12. Claims 93-103 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10-20, 27-29, and 40-53 of copending Application No. 09/791,153 in view of WO 93/12227 (of record as reference BC on the 3/25/99 IDS).

The claims of copending application 09/791,153 recite antibodies comprising specific Fab sequences that bind human OPGbp, and indicate that these antibodies comprise human Fc domains (see particularly claims 12 and 13). These claims differ from the instant invention in that they do not teach that the antibodies of a defined sequence (i.e. monoclonal) are human.

The '227 patent teaches that human antibodies offer an advantage over all other antibody type for *in vivo* diagnostic and therapeutic use in that the use of human antibodies reduces anti-therapeutic antibody responses, including HAMA responses (see particularly page 1, lines 27-38). Such responses are generated due to the inherent immunogenicity of non-human immunoglobulins. When non-human antibodies are administered to a human patient, the patient's immune system produces antibodies that neutralize the efficacy of the therapeutic antibodies, and the resulting antibody complexes can also cause acute toxicity (see particularly page 1, lines 27-38). Human antibodies would not be highly immunogenic in human patients, and as such unwanted anti-antibody responses could be reduced (see particularly page 1, lines 27-38).

Therefore, a person of ordinary skill in the art would have been motivated to make the antibodies recited in the claims of copending application 09/791,153 as human antibodies to gain the advantage of having an antibody of very low immunogenicity that does not elicit unwanted anti-therapeutic antibody responses in the patient such that it can be used in methods of administration to human patients.

This is a provisional obviousness-type double patenting rejection.

13. Claims 93-103 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 80-91 of copending application 11/981,664. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of issued patent anticipate the instant invention. Specifically, the issued claims are drawn to a specific antibody species recited by SEQ ID number whereas the instant claims are drawn to a broad genus of antibodies which comprise the same functional properties as the antibodies of the copending claims. Note that application 11/981,664 is a continuation of US Patent 7,364,736.

This is a provisional obviousness-type double patenting rejection.

14. Applicant's arguments filed October 14, 2008 have been fully considered but they are not persuasive. Applicant repeats arguments already of record that since the instant application has the earliest priority date, none of the previously identified copending applications qualify as art and thus the double patenting rejections should be withdrawn.

This argument is not persuasive. Specifically, the guidance in the MPEP concerning issuance of the senior application is applicable only when the remaining rejections are *provisional* ODP rejections. Application 10/180,648 issued as US Patent 7,364,736 on April 29, 2008 and thus that rejection is no longer provisional. Since this rejection remains, the other provisional ODP rejections also have been maintained since they too may potentially mature into issued patents at a later time.

***Claim Objections***

15. Claims 93 and 103 are objected to in that they appear to be missing the word "protein" between "osteoprotegerin binding" and "of SEQ ID NO:". Appropriate amendment of the claims is suggested.

16. No claims are allowable.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is (571)272-2934. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Primary Examiner
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